

# **ADVANCED ORGANIC CHEMISTRY**

**REACTIONS,  
MECHANISMS, AND  
STRUCTURE**

**FOURTH EDITION**

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the carbonyl group, and the rate increases because moving the double bond from the 7 to the 6 position causes a change in conformational the carbonyl group (the difference in the side chain at C-17 does not affect the rate).

### Quantitative Treatments of the Effect of Structure on Reactivity<sup>18</sup>

Suppose a reaction is performed on a substrate molecule that can be represented as  $XGY$ , where  $Y$  is the site of the reaction,  $X$  a variable substituent, and  $G$  a skeleton group to which  $X$  and  $Y$  are attached, and we find that changing  $X$  from  $H$  to  $C_6H_5$  results in a rate increase by a factor, say, 10. We would like to know just what part of the increase is due to each of the effects previously mentioned. The obvious way to approach such a problem is to try to find compounds in which one or two of the factors are absent or at least negligible. This is not easy to do acceptably because factors that seem negligible to one investigator do not always appear so to another. The first attempt to give numerical values was that of Hammett.<sup>19</sup> For the cases of *m*- and *p*- $XC_6H_4Y$ , Hammett set up the equation

$$\log \frac{k}{k_0} = \rho \sigma$$

where  $k_0$  is the rate constant or equilibrium constant for  $X = H$ ,  $k$  is the constant for the group  $X$ ,  $\rho$  is a constant for a given reaction under a given set of conditions, and  $\sigma$  is a constant characteristic of the group  $X$ . The equation is called the *Hammett equation*.

The value of  $\rho$  was set at 1.00 for ionization of  $XC_6H_4COOH$  in water at 25°C.  $\sigma_m$  and  $\sigma_p$  values were then calculated for each group (for a group  $X$ ,  $\sigma$  is different for the meta and para positions). Once a set of  $\sigma$  values was obtained,  $\rho$  values could be obtained for other reactions from the rates of just two  $X$ -substituted compounds, if the  $\sigma$  values of the  $X$  groups were known (in practice, at least four well-spaced values are used to calculate  $\rho$  because of experimental error and because the treatment is not exact). With the  $\rho$  value thus calculated and the known  $\sigma$  values for other groups, rates can be predicted for reactions that have not yet been run.

The  $\sigma$  values are numbers that sum up the total electrical effects (resonance plus field) of a group  $X$  when attached to a benzene ring. The treatment usually fails for the ortho-position. The Hammett treatment has been applied to many reactions and to many functional groups and correlates quite well an enormous amount of data. Jaffé's review article<sup>20</sup> lists  $\rho$  values for 204 reactions,<sup>21</sup> many of which have different  $\rho$  values for different conditions.

<sup>18</sup>For monographs, see Exner *Correlation Analysis of Chemical Data*; Plenum, New York, 1988; Johnson *The Hammett Equation*; Cambridge University Press, Cambridge, 1973; Shriver *Correlation Analysis of Organic Reactivity*; Wiley, New York, 1982; *Correlation Analysis in Organic Chemistry*; Clarendon Press, Oxford, 1973; Chapman *Shorter Correlation Analysis in Chemistry: Recent Advances*; Plenum, New York, 1978; *Advances in Linear Free Energy Relationships*; Plenum, New York, 1972; Wells *Linear Free Energy Relationships*; Academic Press, New York, 1968. For reviews, see Connors *Chemical Kinetics*; VCH, New York, 1990, pp. 311-313; Lewis, in Bernasek *Investigation of Rates and Mechanisms of Reactions* (vol. 6 of Weissberger *Techniques of Chemistry*), 4th ed.; Wiley, New York, 1986, pp. 371-381; Hammett, Ref. 2, pp. 347-381; Jones *Physical and Mechanistic Organic Chemistry*, 2nd ed.; Cambridge University Press, Cambridge, 1984, pp. 38-68; Charlton, *CHEMTECH* 1974, 362-311, 1975, 243-255; Hine *Structural Effects in Organic Chemistry*; Wiley, New York, 1975, pp. 55-102; Atanasov *Russ. Chem. Rev.* 1971, 49, 216-232; Laurent, *Wojtkowicz Ann. Chim. (Paris)* 1979, [16] 5, 163-191. For a historical perspective, see Grunwaldt *CHEMTECH* 1988, 498.

<sup>19</sup>For a review, see Jaffé *Chem. Rev.* 1983, 53, 191.

<sup>20</sup>Additional  $\rho$  values are given in Wells *Chem. Rev.* 1963, 63, 173-218 and van Nekkum, Verkade, Wepster *Rec. Trav. Chim. Pays-Bas* 1989, 78, 821-827.

double bond from the 7 to group (the difference in the activity<sup>15</sup>

can be represented as  $XGY$ , and  $G$  a skeleton group to  $H$  to  $CH_3$ , results in a rate part of the increase is due to approach such a problem absent or at least negligible, eligible to one investigator numerical values was that of the equation:

$\frac{1}{k} = k \cdot \text{constant for the } \sigma \text{ of conditions, and } \sigma \text{ is a Hammett equation.}$   
In water at 25°C,  $\sigma_m$  and  $\sigma$  is different for the meta values could be obtained for ands, if the  $\sigma$  values of the es are used to calculate  $\rho$  (exact). With the  $\rho$  value to be predicted for reactions

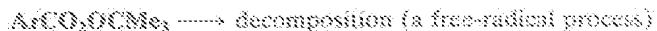
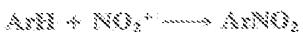
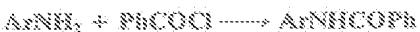
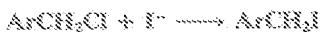
fects (resonance plus field) usually fails for the ortho ands and to many functional Jaffé's review article<sup>16</sup> lists es for different conditions.

<sup>15</sup> New York, 1988; Johnson *The Ion Analysis of Organic Reactivity*; Oxford, 1973; Chapman; Shorter *Advances in Linear Free Energy Academic Press; New York, 1968; Lewis, in Bernasconi *Investigations* (4th ed.), Wiley; New York, 1978; *Organic Chemistry*, 2nd ed., 974, 502-511, 1978, 285-295; Hinczey *Russ. Chem. Rev.* 1971, 49, torsional perspective, see Grunwald*

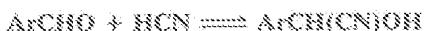
Bekkum; Verkade; Weesper Rec.

Among them are reactions as disparate as the following:

Rate constants for



Equilibrium constants for



The Hammett equation has also been shown to apply to many physical measurements, including ir frequencies and nmr chemical shifts.<sup>18</sup> The treatment is reasonably successful whether the substrates are attacked by electrophilic, nucleophilic, or free-radical reagents, the important thing being that the mechanism be the same *within* a given reaction series.

However, there are many reactions that do not fit the treatment. These are mostly reactions where the attack is directly on the ring and where the  $X$  group can enter into direct resonance interaction with the reaction site in the transition state (that is, the substrate is  $XY$  rather than  $XGY$ ). For these cases, two new sets of  $\sigma$  values have been devised:  $\sigma'$  values (proposed by H. C. Brown) for cases in which an electron-donating group interacts with a developing positive charge in the transition state (this includes the important case of electrophilic aromatic substitutions; see Chapter 11), and  $\sigma''$  values, where electron-withdrawing groups interact with a developing negative charge. Table 9.4 gives  $\sigma$ ,  $\sigma'$ , and  $\sigma''$  values for some common  $X$  groups.<sup>19</sup> As shown in the table,  $\sigma$  is not very different from  $\sigma'$  for most electron-withdrawing groups.  $\sigma_m''$  values are not shown in the table, since they are essentially the same as the  $\sigma_m'$  values.

A positive value of  $\sigma$  indicates an electron-withdrawing group and a negative value an electron-donating group. The constant  $\rho$  measures the susceptibility of the reaction to electrical effects.<sup>20</sup> Reactions with a positive  $\rho$  are helped by electron-withdrawing groups and vice versa. The following  $\rho$  values for the ionization of some carboxylic acids illustrate this:<sup>21</sup>

$\text{XC}_6\text{H}_4-\text{COOH}$	1.00	$\text{XC}_6\text{H}_4-\text{CH}=\text{CH}-\text{COOH}$	0.47
$\text{XC}_6\text{H}_4-\text{CH}_2-\text{COOH}$	0.49	$\text{XC}_6\text{H}_4-\text{CH}_2\text{CH}_2-\text{COOH}$	0.21

<sup>18</sup> For a review of Hammett treatment of nmr chemical shifts, see Ewing, in Chapman; *Shorter Correlation Analysis in Chemistry: Recent Advances*; Plenum, New York, 1978, pp. 357-396.

<sup>19</sup> Unless otherwise noted,  $\sigma$  values are from Exner, in Chapman; Shorter, Ref. 18, pp. 439-540, and  $\sigma'$  values from Okamoto; Inukai; Brown *J. Am. Chem. Soc.* 1988, 89, 4969; and Brown; Okamoto *J. Am. Chem. Soc.* 1958, 80, 4979.  $\sigma''$  values, except as noted, are from Jaffé, Ref. 16. Exner, pp. 439-540, has extensive tables giving values for more than 300 groups, as well as  $\sigma'$ ,  $\sigma''$ ,  $\sigma_D$ ,  $\sigma_B$ , and  $\sigma_L$  values for many of these groups. Other large tables of the various sigma values are found in Hansch; Leo; *Tetrahedron*, 1981, 37, 183-195. For tables of  $\sigma_p$ ,  $\sigma_m$ ,  $\sigma''$ ,  $\sigma_D$ , and  $\sigma_B$  values of many groups containing Si, Ge, Sn, and Pb atoms, see Egorushkin; Razuvaev *Russ. Chem. Rev.* 1987, 56, 848-858. For values for heteroaromatic groups, see Mamaev; Shikurko; *Baran Adv. Heterocycl. Chem.* 1987, 42, 1-82.

<sup>20</sup> For discussions of the precise significance of  $\rho$ , see Dubois; Russia; *Angew. J. Am. Chem. Soc.* 1984, 106, 4849; Russia; Angew. *Dubois J. Am. Chem. Soc.* 1984, 106, 4846; Lee; Shim; Chung; Kim; Lee *J. Chem. Soc., Perkin Trans. 2* 1988, 1819.

<sup>21</sup> Jones, Ref. 18, p. 42.

TABLE 8.4  $\sigma$ ,  $\sigma'$ , and  $\sigma''$  values for some common groups<sup>a</sup>

Group	$\sigma_p$	$\sigma_m$	$\sigma_p''$	$\sigma_m''$	$\sigma_p'''$
$\text{O}^-$	-0.81 <sup>b</sup>	-0.47 <sup>b</sup>	-4.27 <sup>c</sup>	-1.18 <sup>c</sup>	
$\text{NMe}_2$	-0.63	-0.10	-1.7		
$\text{NH}_2$	-0.57	-0.09	-1.3	-0.16	
$\text{OH}$	-0.38 <sup>d</sup>	-0.13 <sup>d</sup>	-0.92 <sup>d</sup>		
$\text{CMe}_3$	-0.28 <sup>d</sup>	0.10	-0.78	0.08	
$\text{CH}_3$	-0.15	-0.09	-0.26	-0.06	
$\text{Me}$	-0.14	-0.06 <sup>e</sup>	-0.31	-0.10 <sup>e</sup>	
H	0	0	0	0	0
Pb	0.05 <sup>f</sup>	0.05	-0.18	0 <sup>f</sup>	
$\text{COO}^-$	0.11 <sup>g</sup>	0.02 <sup>h</sup>	-0.31 <sup>g</sup>	-0.10 <sup>g</sup>	
F	0.15	0.34	-0.07	0.35	
Cl	0.24	0.37	0.11	0.40	
Br	0.26	0.37	0.15	0.41	
I	0.28 <sup>i</sup>	0.34	0.14	0.36	
$\text{N}=\text{NPh}^{j,k}$	0.34	0.28	0.17		
$\text{COOH}$	0.44	0.35	0.42	0.32	0.73
$\text{COOR}$	0.44	0.35	0.48	0.37	0.68
$\text{COMe}$	0.47	0.36			0.67
$\text{CF}_3$	0.53	0.46		0.57 <sup>k</sup>	
$\text{NH}_3^+$	0.60 <sup>l</sup>	0.86 <sup>l</sup>			
$\text{CN}^{m,n}$	0.70	0.62	0.66	0.56	1.30
$\text{SG}_2\text{Me}$	0.73	0.64			
$\text{NO}_2$	0.81	0.71	0.79	0.72 <sup>o</sup>	1.27
$\text{NMe}_2^+$	0.82 <sup>p</sup>	0.88 <sup>q</sup>	0.41	0.38	
$\text{N}_3^+$	1.93 <sup>r</sup>	1.65 <sup>r</sup>	1.88 <sup>r</sup>		3 <sup>r</sup>

This example shows that the insertion of a  $\text{CH}_2$  or a  $\text{CH}=\text{CH}$  group diminishes electrical effects to about the same extent, while a  $\text{CH}_2\text{CH}_2$  group diminishes them much more. A  $\rho$  greater than 1 would mean that the reaction is more sensitive to electrical effects than is the ionization of  $\text{XC}_6\text{H}_4\text{COO}^-$  ( $\rho = 1.00$ ).

Similar calculations have been made for compounds with two groups X and X' on one ring, where the  $\sigma$  values are sometimes additive and sometimes not,<sup>20</sup> for other ring systems such as naphthalene<sup>21</sup> and heterocyclic rings,<sup>22</sup> and for ethylenic and acetylenic systems.<sup>23</sup>

<sup>a</sup>Nishimi; Ko; Hepler *Can. J. Chem.* 1974, 52, 2908.<sup>b</sup>de la Mare; Newman *Tetrahedron Lett.* 1963, 1365; give this value as -1.6.<sup>c</sup>Amin; Taylor *Tetrahedron Lett.* 1978, 297.<sup>d</sup>Sjöstrand; Wold *Chem. Scr.* 1976, 9, 209.<sup>e</sup>Byrne; Happer; Hartshorn; Powell *J. Chem. Soc., Perkin Trans. 2* 1987, 1849.<sup>f</sup>For a review of directing and activating effects of  $\text{C}\equiv\text{O}$ ,  $\text{C}\equiv\text{C}$ ,  $\text{C}\equiv\text{N}$ , and  $\text{C}\equiv\text{S}$  groups, see Charton, in Patai *The Chemistry of Double-bonded Functional Groups*, vol. 2, pt. 1; Wiley: New York, 1989, pp. 239-298.<sup>g</sup>For a review of directing and activating effects of CN and  $\text{C}\equiv\text{C}$  groups, see Charton, in Patai; Rappoport *The Chemistry of Functional Groups, Supplement C*, pt. 1; Wiley: New York, 1983, pp. 269-323.<sup>h</sup>McDaniell; Brown *J. Org. Chem.* 1958, 23, 429.<sup>i</sup>Ulyanuk; Sudbeekin; Buchneva; Grusdova; Kazitsyna *Doklad. Chem.* 1976, 227, 179.<sup>j</sup>Lewis; Johnson *J. Am. Chem. Soc.* 1939, 61, 3079.<sup>k</sup>Hine *J. Am. Chem. Soc.* 1889, 11, 4877.<sup>l</sup>Binev; Kuzmanova; Kanev; Iuchimovski *J. Chem. Soc., Perkin Trans. 2* 1982, 1833.<sup>m</sup>Stone; Pearson *J. Org. Chem.* 1961, 26, 257.<sup>n</sup>Berlinar; Whilcox *J. Am. Chem. Soc.* 1959, 81, 1630; see also Wells; Ehrenson, *Text. Ref.* 38.<sup>o</sup>For reviews, see Charton, in Chapman; Shoer, *Ref.* 18, pp. 175-268; Tomasko; Johnson *Adv. Heterocycl. Chem.* 1978, 28, 1-83.<sup>p</sup>For reviews of the application of the Hammett treatment to unsaturated systems, see Ford; Kutzinsky; Bigelow, in Chapman; Shoer, *Ref.* 18, pp. 269-311; Cisneros *Prog. Phys. Org. Chem.* 1973, 10, 33-204.

The Hammett equation is a *linear free-energy relationship (LFER)*. This can be demonstrated as follows for the case of equilibrium constants (for rate constants a similar demonstration can be made with  $\Delta G'$  instead of  $\Delta G$ ). For each reaction, where X is any group,

$$\Delta G = -RT \ln K$$

For the unsubstituted case,

$$\Delta G_0 = -RT \ln K_0$$

The Hammett equation can be rewritten

$$\log K - \log K_0 = \alpha \rho$$

so that

$$\frac{-\Delta G}{2.3RT} + \frac{\Delta G_0}{2.3RT} = \alpha \rho$$

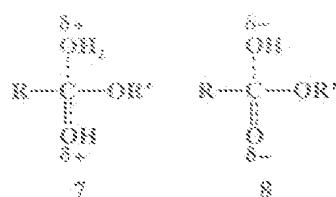
and

$$-\Delta G = \alpha \rho 2.3RT - \Delta G_0$$

For a given reaction under a given set of conditions,  $\alpha$ , R, T, and  $\Delta G_0$  are all constant, so that  $\rho$  is linear with  $\Delta G$ .

The Hammett equation is not the only LFER.<sup>27</sup> Some, like the Hammett equation, correlate structural changes in reactants, but the Grunwald-Winstein relationship (see p. 360) correlates changes in solvent and the Brønsted relation (see p. 238) relates acidity to catalysis. The Taft equation is a structure-reactivity equation that correlates only field effects.<sup>28</sup>

Taft, following Ingold,<sup>29</sup> assumed that for the hydrolysis of carboxylic esters, steric and resonance effects will be the same whether the hydrolysis is catalyzed by acid or base (see the discussion of ester-hydrolysis mechanisms, reaction 9-10). Rate differences would therefore be caused only by the field effects of R and R' in  $\text{RCOOR}'$ . This is presumably a good system to use for this purpose because the transition state for acid-catalyzed hydrolysis (7) has a greater positive charge (and is hence destabilized by  $-I$  and stabilized by  $+I$  substituents) than the starting ester, while the transition state for base-catalyzed hydrolysis (8)



(*for a discussion of physicochemical preconditions for LFERs, see Sünner *Prog. Phys. Org. Chem.* 1998, 17, 129-161.*)

*For reviews of the separation of resonance and field effects, see Charlton *Prog. Phys. Org. Chem.* 1981, 12, 349-381; Shorter *J. Rev. Chem. Soc. (London)* 1978, 24, 431-453; *Chem. Br.* 1969, 5, 266-274. For a review of field and inductive effects, see Reynolds *Prog. Phys. Org. Chem.* 1983, 14, 165-203. For a review of field effects on reactivity, see *Gesell Amer. Chem. Inst. Ed. Engl.* 1978, 15, 569-575 [*Angew. Chem. Int. Ed.* 1978, 17, 613-627].*

<sup>27</sup>Ingold *J. Chem. Soc.* 1933, 1632.

<sup>28</sup>For another set of field-steric correlations, based on a different premise, see Dreiding, Pinnick *J. Phys. Chem.* 1978, 12, 249.

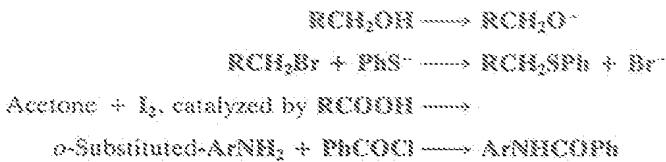
has a greater negative charge than the starting ester. Field effects of substituents X could therefore be determined by measuring the rates of acid- and base-catalyzed hydrolysis of a series  $XCH_2COOR'$ , where  $R'$  is held constant.<sup>25</sup> From these rate constants, a value  $\sigma_f$  could be determined by the equation:<sup>26</sup>

$$\sigma_f \equiv 0.181 \left[ \log \left( \frac{k}{k_0} \right)_B - \log \left( \frac{k}{k_0} \right)_A \right]$$

In this equation  $(k/k_0)_B$  is the rate constant for basic hydrolysis of  $XCH_2COOR'$  divided by the rate constant for basic hydrolysis of  $CH_3COOR'$ ;  $(k/k_0)_A$  is the similar rate-constant ratio for acid catalysis, and 0.181 is an arbitrary constant.  $\sigma_f$  is a substituent constant for a group X, substituted at a saturated carbon, that reflects only field effects.<sup>27</sup> Once a set of  $\sigma_f$  values was obtained, it was found that the equation

$$\log \frac{k}{k_0} = \rho_f \sigma_f$$

holds for a number of reactions, among them:<sup>28</sup>



As with the Hammett equation,  $\sigma_f$  is constant for a given reaction under a given set of conditions. For very large groups the relationship may fail because of the presence of steric effects, which are not constant. The equation also fails when X enters into resonance with the reaction center to different extents in the initial and transition states. A list of some  $\sigma_f$  values is given in Table 9.5.<sup>29</sup> The  $\sigma_f$  values are about what we would expect for pure field-effect values (see p. 18) and are additive, as field effects (but not resonance or steric effects) would be expected to be. Thus, in moving a group one carbon down the chain, there is a decrease by a factor of  $2.8 \pm 0.5$  (compare the values of R and  $CH_2$  in Table 9.5 for  $B = Ph$  and  $CH_3CO$ ). An inspection of Table 9.5 shows that  $\sigma_f$  values for most groups are fairly close to the  $\sigma_m$  values (Table 9.4) for the same groups. This is not surprising, since  $\sigma_m$  values would be expected to arise almost entirely from field effects, with little contribution from resonance.

Since  $\sigma_f$  values represent the sum of resonance and field effects, these values can be divided into resonance and field contributions if  $\sigma_f$  is taken to represent the field-effect

<sup>26</sup>The symbol  $\sigma_F$  is also used in the literature; sometimes in place of  $\sigma_f$ , and sometimes to indicate only the field (not the inductive) portion of the total effect (p. 17).

<sup>27</sup>There is another set of values (called  $\sigma^*$  values) that are also used to correlate field effects. These are related to  $\sigma_f$  values by  $= \sigma_{fx} = 0.45\sigma_f^{0.75}$ . We discuss only  $\sigma_f$ , and not  $\sigma^*$  values.

<sup>28</sup>Wells, Ref. 17, p. 196.

<sup>29</sup>These values are from Bromilow; Brownlee; Lopez; Tsit, Ref. 22, except that the values for  $NHAc$ ,  $OH$ , and  $I$  are from Wells; Ehrsson; Tait, Ref. 48, the values for  $Ph$  and  $NMe_2$  are from Ref. 51 and Tait; Deno; Skell, Ref. 47, and the value for  $CMes$  is from Seth-Paul; de Meyer-van Duyse; Tollenraad *J. Mol. Struct.*, 1973, 19, 811. The values for the  $CH_2Ph$  and  $CH_2COCH_3$  groups were calculated from  $\sigma^*$  values by the formula given in footnote 22. For much larger tables of  $\sigma_f$  and  $\sigma_m$  values, see Charlton, Ref. 38. See also Ref. 19 and Taylor; Wahl *J. Chem. Soc., Perkin Trans. 2* 1988, 1763.

of substituents X could catalyze hydrolysis of a  $\beta$ -keto ester, a value  $\sigma_i$

$\delta XCH_2COOR'$  divided the similar rate-constant substituent constant for  $\alpha$ -effects.<sup>52</sup> Once a set of

TABLE 9.5  $\sigma_i$  and  $\sigma_R^*$  values for some groups<sup>53</sup>

Group	$\sigma_i$	$\sigma_R^*$	Group	$\sigma_i$	$\sigma_R^*$
$CMes_2$	~0.07	~0.17	OMe	0.27	~0.42
Me	~0.05	~0.13	OH	0.27	~0.44
H	0	0	I	0.39	~0.12
$PhCH_2$	0.04		$CF_3$	0.42	0.08
$NMe_2^{+}$	0.06	~0.55	Br	0.44	~0.16
Ph	0.10	~0.10	Cl	0.46	~0.18
$CH_3COCH_3$	0.18		F	0.50	~0.31
$NH_2$	0.12	~0.50	CN	0.56	0.08
$CH_3CO$	0.20	0.16	$SO_2Me$	0.60	0.12
$COOEt$	0.20	0.16	$NO_2$	0.65	0.15
$NHAc$	0.26	~0.22	$NMe_2^{+}$	0.86	

portion.<sup>57</sup> The resonance contribution  $\sigma_R^{**}$  is defined as

$$\sigma_R = \sigma_p - \sigma_i$$

As it stands, however, this equation is not very useful because the  $\sigma_R$  value for a given group, which should be constant if the equation is to have any meaning, is actually not constant but depends on the nature of the reaction.<sup>58</sup> In this respect, the  $\sigma_i$  values are much better. Although they vary with solvent in some cases,  $\sigma_i$  values are essentially invariant throughout a wide variety of reaction series. However, it is possible to overcome<sup>59</sup> the problem of varying  $\sigma_R$  values by using a special set of  $\sigma_R$  values, called  $\sigma_R^*$ ,<sup>60</sup> that measure the ability to delocalize  $\pi$  electrons into or out of an unperturbed or "neutral" benzene ring. Several  $\sigma_R^*$  scales have been reported; the most satisfactory values are obtained from  $^{13}C$  chemical shifts of substituted benzenes.<sup>61</sup> Table 9.5 lists some values of  $\sigma_R^*$ , most of which were obtained in this way.<sup>62</sup>

An equation such as

$$\log \frac{k}{k_0} = \rho \sigma_i + \rho \sigma_R^*$$

<sup>57</sup>For  $\sigma_R^*$  values for some other  $NR_2$  groups, see Korzhenevskaya, Tsvov, Chotti, Chekhman, *J. Org. Chem. USSR*, 1987, 28, 1169.

<sup>58</sup>Although we give a  $\sigma_i$  value for  $NMe_2^+$ , (and  $F$  values for three charged groups in Table 9.6), it has been shown that charged groups (called polar substituents) cannot be included with uncharged groups (dipolar substituents) in one general scale of electrical substituent effects: Marriott; Reynolds; Topsom, *J. Org. Chem.*, 1988, 53, 741.

<sup>59</sup>Roberts; Moreland, *J. Am. Chem. Soc.*, 1953, 75, 2167; Taft, *J. Am. Chem. Soc.*, 1957, 79, 1043; *J. Phys. Chem.*, 1960, 64, 1805; Taft; Lewis, *J. Am. Chem. Soc.*, 1958, 80, 2436; Taft; Deno; Skell, *Ann. Rev. Phys. Chem.*, 1958, 9, 287-314, pp. 290-293.

<sup>60</sup>For reviews of the  $\sigma_i$  and  $\sigma_R$  concept as applied to benzenes and naphthalenes, respectively, see Ehrenson; Brownlee; Taft, *Prog. Phys. Org. Chem.*, 1973, 10, 1-80; Wells; Ehrenson; Taft, *Prog. Phys. Org. Chem.*, 1968, 8, 147-322. See also Taft; Topsom, *Prog. Phys. Org. Chem.*, 1987, 16, 1-83; Charlton, *Prog. Phys. Org. Chem.*, 1987, 16, 287-315.

<sup>61</sup>Taft; Lewis, *J. Am. Chem. Soc.*, 1959, 81, 3343; Reynolds; Dais; MacIntyre; Topsom; Marriott; von Nagy-Fehobuki; Taft, *J. Am. Chem. Soc.*, 1983, 105, 378.

<sup>62</sup>For a different way of overcoming this problem, see Happer; Wright, *J. Chem. Soc., Perkin Trans. 2*, 1979, 693, 397; Ehrenson; Lewis; Glick, *J. Am. Chem. Soc.*, 1989, 81, 5352.

<sup>63</sup>Brimlow; Brownlee; Lopez; Taft, *J. Org. Chem.*, 1978, 44, 4766. See also Marriott; Topsom, *J. Chem. Soc., Perkin Trans. 2*, 1988, 1045.

<sup>64</sup>For a set of  $\sigma_R$  values for use in  $XY^+$  systems, see Charlton, *Mol. Struct. Energ.*, 1987, 4, 271-217.

## OPh

on under a given set of of the presence of steric factors into resonance with states. A list of some  $\sigma_i$  would expect for pure t noj resonance or steric carbon down the chain, of R and  $RCH_2$  in Table that  $\sigma_i$  values for most ps. This is not surprising, field effects, with little

cis, these values can be present the field-effect

times to indicate only the field field effects. These are related

the values for NHAc, OH, and Ref. 51 and Taft; Deno; Skell, *e. J. Mol. Struct.*, 1973, 19, 811, y the formulae given in footnote 19 and Taylor, *Walt J. Chem.*

which treats resonance and field effects separately, is known as a *dual substituent parameter equation*.<sup>54</sup>

The only groups in Table 9.5 with negative values of  $\sigma_f$  are the alkyl groups methyl and *t*-butyl. There has been some controversy on this point.<sup>55</sup> One opinion is that  $\sigma_f$  values decrease in the series methyl, ethyl, isopropyl, *t*-butyl (respectively, -0.046, -0.057, -0.065, -0.074).<sup>56</sup> Other evidence, however, has led to the belief that all alkyl groups have approximately the same field effect and that the  $\sigma_f$  values are invalid as a measure of the intrinsic field effects of alkyl groups.<sup>57</sup>

Another attempt to divide  $\sigma$  values into resonance and field contributions<sup>58</sup> is that of Swain and Lupton, who have shown that the large number of sets of  $\sigma$  values ( $\sigma_m$ ,  $\sigma_p$ ,  $\sigma_p''$ ,  $\sigma_p'''$ ,  $\sigma_f$ ,  $\sigma_R$ , etc., as well as others we have not mentioned) are not entirely independent and that linear combinations of two sets of new values  $F$  (which expresses the field-effect contribution) and  $R$  (the resonance contribution) satisfactorily express 43 sets of values.<sup>59</sup> Each set is expressed as

$$\sigma = fF + rR$$

where  $f$  and  $r$  are weighting factors. Some  $F$  and  $R$  values for common groups are given in Table 9.6.<sup>60</sup> From the calculated values of  $f$  and  $r$ , Swain and Lupton calculated that the

TABLE 9.6.  $F$  and  $R$  values for some groups<sup>60</sup>

Group	$F$	$R$	Group	$F$	$R$
COO <sup>-</sup>	-0.27	0.49	OMe	0.54	-1.68
Me <sub>2</sub> C	-0.31	-0.29	CF <sub>3</sub>	0.64	-0.76
Et	-0.02	-0.44	I	0.65	-0.12
Me	-0.01	-0.41	Br	0.72	-0.18
H	0	0	Cl	0.72	-0.24
Ph	0.25	-0.37	S	0.74	-0.60
NH <sub>2</sub>	0.38	-2.52	NHCOCH <sub>3</sub>	0.77	-1.43
COOH	0.44	0.66	CN	0.90	-0.71
OH	0.46	-1.89	NMe <sub>2</sub> <sup>+</sup>	1.54	
COOEt	0.47	0.67	N <sub>2</sub> <sup>+</sup>	2.36	2.81
COCH <sub>3</sub>	0.50	0.89			

<sup>54</sup>There are also three-parameter equations. See, for example, da Ligny and van Rouwelingen, *J. Chem. Soc., Perkin Trans. 2* 1987, 559.

<sup>55</sup>For a discussion, see Shorter, in Chapman; Shorter, *Advances in Linear Free Energy Relationships*, Ref. 15, pp. 98-103.

<sup>56</sup>For support for this point of view, see Levitt; Wilding, *Prog. Phys. Org. Chem.* 1976, 12, 119-157; Taft; Levitt, *J. Org. Chem.* 1977, 42, 916; MacPhee; Dubois, *Tetrahedron Lett.* 1978, 2225; Serettas *J. Org. Chem.* 1979, 44, 3332; Hanson *J. Chem. Soc., Perkin Trans. 2* 1984, 101.

<sup>57</sup>For support for this point of view, see, for example, Ritchie *J. Phys. Chem.* 1961, 65, 2091; Bondwell; Drucker; McCollum *J. Org. Chem.* 1976, 41, 2786; Bondwell; Fried, *Tetrahedron Lett.* 1977, 1121; Charlton *J. Am. Chem. Soc.* 1977, 99, 5687; *J. Org. Chem.* 1979, 44, 903; Adcock; Khor *J. Org. Chem.* 1978, 43, 1272; DeTa *J. Org. Chem.* 1988, 53, 5166; *J. Am. Chem. Soc.* 1988, 110, 7988.

<sup>58</sup>Yukawa and Tsuno have still another approach, also involving dual parameters. Yukawa; Tsuno, *Bull. Chem. Soc. Jpn.* 1959, 32, 971. For a review and critique of this method, see Shorter, in Chapman; Shorter, Ref. 15, pp. 119-173, pp. 136-144. This article also discusses the Swain-Lupton and Taft  $\sigma$ ,  $\pi$ , approaches. For yet other approaches, see Almas'ev *J. Org. Chem. USSR* 1981, 17, 373; *J. Chem. Soc., Perkin Trans. 2* 1984, 1389; Ponec *Coll. Czech. Chem. Commun.* 1983, 48, 1564.

<sup>59</sup>Swain; Lupton *J. Am. Chem. Soc.* 1968, 90, 4328; Swain; Unger; Rosenquist; Swain, *J. Am. Chem. Soc.* 1983, 105, 492.

<sup>60</sup>Taken from a much longer list in Swain; Unger; Rosenquist; Swain, Ref. 59. Long tables of  $R$  and  $F$  values are also given in Hansch; Leo; Taft, Ref. 19.

*i* substituent parameter

alkyl groups methyl and isopropyl is that  $\sigma_f$  values for  $\text{CH}_3$ ,  $\sim 0.046$ ,  $\sim 0.057$ ,  $\text{t}$  that all alkyl groups are valid as a measure of

contribution<sup>53</sup> is that of  $\sigma$  values ( $\sigma_m$ ,  $\sigma_p$ ,  $\sigma_{p'}$ ), it entirely independent of pressure or field-effect terms<sup>54</sup> 43 sets of values.<sup>55</sup>

ion groups are given in ion calculated that the

importance of resonance, %  $R$ , is 20% for  $\sigma_m$ , 38% for  $\sigma_p$ , and 62% for  $\sigma_{p'}$ .<sup>53</sup> This is another dual substituent parameter approach.

Taft was also able to isolate steric effects.<sup>56</sup> For the acid-catalyzed hydrolysis of esters in aqueous acetone,  $\log(k/k_0)$  was shown to be insensitive to polar effects.<sup>57</sup> In cases where resonance interaction was absent, this value was proportional only to steric effects (and any others<sup>58</sup> that are not field or resonance). The equation is

$$\log \frac{k}{k_0} = E_s$$

Some  $E_s$  values are given in Table 9.7,<sup>59</sup> where hydrogen is taken as standard, with a value of 0.<sup>60</sup> This treatment is more restricted than those previously discussed, since it requires more assumptions, but the  $E_s$  values are approximately in order of the size of the groups. Charlton has shown that  $E_s$  values for substituents of types  $\text{CH}_2\text{X}$ ,  $\text{CHX}_2$ , and  $\text{CX}_3$  are linear functions of the van der Waals radii for these groups.<sup>61</sup>

Two other steric parameters are independent of any kinetic data. Charlton's  $v$  values are derived from van der Waals radii,<sup>62</sup> and Meyer's  $V^*$  values from the volume of the portion of the substituent that is within 0.3 nm of the reaction center.<sup>63</sup> The  $V^*$  values are obtained by molecular mechanics calculations based on the structure of the molecule. Table 9.7 gives  $v$  and  $V^*$  values for some groups.<sup>59</sup> As can be seen in the table, there is a fair, but not

TABLE 9.7  $E_s$ ,  $v$ , and  $V^*$  values for some groups<sup>59</sup>

$R$	$E_s$	$v$	$V^* \times 10^3$	$R$	$E_s$	$v$	$V^* \times 10^3$
4	-1.68			H	0	0	
4	0.76			F	-0.46	0.27	1.22
5	-0.12			CN	-0.51		
2	-0.18			ON	-0.55		
2	-0.24			OMe	-0.55		3.39
4	-0.60			NH <sub>2</sub>	-0.61		
7	-1.43			Cl	-0.97	0.55	2.54
0	0.71			Me	-1.24	0.52	2.84
4				Et	-1.31	0.56	4.31
6	2.81			I	-1.4	0.78	4.08
				Pr	-1.6	0.68	4.78
				iso-Pr	-1.71	0.76	5.74
				Cyclohexyl	-2.03	0.87	6.25
				iso-Bu	-2.17	0.98	5.26
				sec-Bu	-2.37	1.02	6.21
				CF <sub>3</sub>	-3.4	0.91	3.54
				t-Bu	-2.78	1.24	7.16
				NMe <sub>3</sub> <sup>+</sup>	-2.84		
				Neopentyl	-2.98	1.34	8.75
				CCl <sub>3</sub>	-3.3	1.38	6.43
				CHBr <sub>3</sub>	-3.67	1.36	7.29
				(Me <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> CH	-4.42	2.03	
				Et <sub>2</sub> C	-5.04	2.38	
				Ph <sub>2</sub> C	-5.92	3.92	

<sup>53</sup>The Swain-Logp treatment has been criticized by Reynolds; Topsom *J. Org. Chem.*, 1984, **49**, 1969; Hoefnagel; Oosterbeek; Weijter *J. Org. Chem.*, 1984, **49**, 1993; and Charlton *J. Org. Chem.*, 1984, **49**, 1997. For a reply to these criticisms, see Swain *J. Org. Chem.*, 1984, **49**, 2005. A study of the rates of dediazoation reactions (3-23) was more in accord with the Taft and Charlton (Ref. 58)  $\sigma_f$  and  $\sigma_g$  values than with the Swain-Logp  $F$  and  $R$  values; Nakazumi; Kitao; Zollinger *J. Org. Chem.*, 1987, **52**, 2825.

<sup>54</sup>For reviews of quantitative treatments of steric effects, see Gallo; Rousset; Berg *Adv. Heterocycl. Chem.*, 1988, **43**, 173-299; Gallo *Prog. Phys. Org. Chem.*, 1983, **18**, 115-163; Unger; Hansch *Prog. Phys. Org. Chem.*, 1976, **12**, 91-118.

<sup>55</sup>Another reaction used for the quantitative measurement of steric effects is the aminolysis of esters (8-55); De Tar; Delahunt *J. Am. Chem. Soc.*, 1983, **105**, 2734.

<sup>56</sup>It has been shown that  $E_s$  values include solvation effects; McClelland; Sweenken *J. Am. Chem. Soc.*, 1988, **110**, 3860.

<sup>57</sup> $E_s$ ,  $v$ , and  $V^*$  values are taken from longer tables in respectively, Ref. 62; Charlton *J. Am. Chem. Soc.*, 1978, **97**, 1552; *J. Org. Chem.*, 1976, **41**, 2217; and Ref. 69.

<sup>58</sup>In Taft's original work, Me was given the value 0. The  $E_s$  values in Table 9.7 can be converted to the original values by adding 1.24.

<sup>59</sup>Charlton *J. Am. Chem. Soc.*, 1969, **91**, 618.

<sup>60</sup>Charlton, Ref. 65. See also Charlton *J. Org. Chem.*, 1978, **43**, 3975; idem; Schreck *J. Org. Chem.*, 1978, **43**, 4032.

<sup>61</sup>Meyer *J. Chem. Soc., Perkin Trans. 2* 1988, 1987.

<sup>62</sup>For a discussion of the various steric parameters, see De Tar, Ref. 57.

perfect correlation among the  $E_s$ ,  $\nu_s$ , and  $V^*$  values. Other sets of steric values, e.g.,  $E_s^*$ ,<sup>71</sup>  $E_s^{\ddagger}$ ,<sup>72</sup>  $\Omega_s^{13}$  and  $S_t$ ,<sup>73</sup> have also been proposed.<sup>70</sup>

Since the Hammett equation has been so successful in the treatment of the effects of groups in the meta and para positions, it is not surprising that attempts have been made to apply it to ortho positions also.<sup>74</sup> The effect on a reaction rate or equilibrium constant of a group in the ortho position is called the *ortho effect*.<sup>75</sup> Despite the many attempts made to quantify ortho effects, so far no set of values commands general agreement. However, the Hammett treatment is successful for ortho compounds when the group Y in *o*-XC<sub>6</sub>H<sub>4</sub>Y is separated from the ring; e.g., ionization constants of *o*-XC<sub>6</sub>H<sub>4</sub>OCH<sub>2</sub>COOH can be successfully correlated.<sup>76</sup>

Linear free-energy relationships can have mechanistic implications. If log ( $k/k_0$ ) is linear with the appropriate  $\sigma$ , it is likely that the same mechanism operates throughout the series. If not, a smooth curve usually indicates a gradual change in mechanism, while a pair of intersecting straight lines indicates an abrupt change,<sup>77</sup> though nonlinear plots can also be due to other causes, such as complications arising from side reactions. If a reaction series follows  $\sigma^+$  or  $\sigma^-$  better than  $\sigma$  it generally means that there is extensive resonance interaction in the transition state.<sup>78</sup>

Information can also be obtained from the magnitude and sign of  $\rho$ . For example, a strongly negative  $\rho$  value indicates a large electron demand at the reaction center, from which it may be concluded that a highly electron-deficient center, perhaps an incipient carbocation, is involved. Conversely, a positive  $\rho$  value is associated with a developing negative charge in the transition state.<sup>79</sup> The  $\sigma\rho$  relationship even applies to free-radical reactions, because free radicals can have some polar character (p. 679), though  $\rho$  values here are usually small (less than about 1.5) whether positive or negative. Reactions involving cyclic transition states (p. 206) also exhibit very small  $\rho$  values.

<sup>71</sup>MacPhee; Panaye; Dubois *Tetrahedron* 1978, **34**, 3553; *J. Org. Chem.* 1988, **53**, 1164; Dubois; MacPhee; Panaye *Tetrahedron Lett.* 1978, 4999; *Tetrahedron* 1986, **42**, 919. See also Datta; Sharma *J. Chem. Res. (S)* 1987, 422.

<sup>72</sup>Felton; Lust *J. Am. Chem. Soc.* 1973, **95**, 5593.

<sup>73</sup>Komatsu; Sakakibara; Hirota *Tetrahedron Lett.* 1989, **30**, 3309; *Chem. Lett.* 1989, 1913.

<sup>74</sup>Backhaus *Angew. Chem. Int. Ed. Engl.* 1978, **17**, 293 [*Angew. Chem.* 99, 633].

<sup>75</sup>For reviews, see Fujii; Nishizuka *Prog. Phys. Org. Chem.* 1976, **12**, 49-89; Charton *Prog. Phys. Org. Chem.* 1971, **8**, 238-317; Shorter, Ref. 55, pp. 103-110. See also Segura *J. Org. Chem.* 1988, **53**, 1045; Robinson; Norton; Fisher; Jones; Hannessian; Slator *J. Org. Chem.* 1986, **51**, 3535.

<sup>76</sup>This is not the same as the ortho effect discussed on p. 514.

<sup>77</sup>Charton *Can. J. Chem.* 1986, **64**, 2493.

<sup>78</sup>For a discussion, see Schreck *J. Chem. Educ.* 1971, **48**, 103-107.

<sup>79</sup>See, however, Gawley *J. Org. Chem.* 1983, **48**, 4595.

<sup>80</sup>For another method of determining transition state charge, see Williams *Acc. Chem. Res.* 1984, **17**, 425-430.